Development of Appropriate Pediatric Formulations and Drug Delivery Systems

NOTE: The Solicitations and topics listed on this site are copies from the various SBIR agency solicitations and are not necessarily the latest and most up-to-date. For this reason, you should use the agency link listed below which will take you directly to the appropriate agency server where you can read the official version of this solicitation and download the appropriate forms and rules.

The official link for this solicitation is: http://grants.nih.gov/grants/guide/pa-files/PAR-11-305.html

Agency:
Department of Health and Human Services

Release Date:
August 11, 2011
Branch:
n/a

Open Date:
August 11, 2011
Program / Phase / Year:
SBIR / Phase I / 2011

Application Due Date:
September 08, 2014

Solicitation:
PAR-11-305

Close Date:
September 08, 2014
Topic Number:
PAR-11-305

Description:

Purpose

This Funding Opportunity Announcement (FOA) invites Small Business Technology Transfer (STTR) grant applications from small business concerns (SBCs) to address different and complementary research needs for the development appropriate pediatric drug formulations in different age groups. This FOA also encourages the development and testing of novel drug delivery systems in the pediatric population. The goal of this FOA is not to duplicate or compete with the private sector but to complement and accelerate the development of appropriate pediatric drugs formulations and drug delivery systems

Background

The lack of appropriate pediatric formulations has been identified as a major obstacle for the study and use of drugs in children. Pediatric formulations may be inappropriate for different reasons. Children under 12 years of age often have difficulty in swallowing capsules, while those under 4 years generally cannot swallow tablets. Liquid formulations facilitate dose adjustments and are easily administered and are recommended for infants and younger children. The dose and amount of liquid formulations may be limited by the solubility and stability of drugs requiring taste-masking

agents, preservatives and solubility of excipients. Liquid formulations may also not be optimal for the developing world, where clean water and refrigeration may not be available.

In general, there is a need in pediatrics to develop flexible dosage forms that are oro-dispersible or can be prepared as oral liquid formulations. There is an increased recognition that for medicines requiring precise dosage and titration, the development of a universal technology platform could allow for "tailored dosages" and a range of dosage forms for appropriate for children at different developmental stages, or for other populations with swallowing difficulties.

The Biopharmaceutics Classification System (BCS), the scientific framework for classifying drug substances based on their intestinal permeability and solubility/dissolution rates, is widely used to assure bioequivalence of drug products in adults. BCS was developed for bioequivalence studies in adults. Its application in pediatrics has been challenged because the tools used to measure intestinal permeability may not be applicable to young children, as the intestinal mucosa of infants and young children is more permeable than that of adults. In addition, the effects of developmental factors such as gastrointestinal pH, gastrointestinal motility, gastric emptying times and intestinal transport systems on drug bioavailability have not been systematically studied in children.

Driven by federal legislation that now requires evaluation of most drugs in children, renewed attention has been focused on the active pharmaceutical ingredients (APIs). Much less attention has been devoted to the excipients that render these formulations feasible, palatable and, stable

Many APIs are extremely bitter, which can make the development of palatable formulations extremely difficult. Adult formulations are frequently taste masked by coating the tablet or by formulating in a capsule. Young children are often incapable of swallowing tablets or capsules. Because the primary market for most pharmaceuticals is in the adult population where palatability has not been a major consideration, taste masking techniques have not been well developed.

Three broad approaches have been used: 1) to create a barrier between taste receptors and drug (physical coatings, capsules); 2) making chemical or solubility modifications; and 3) to overwhelm the unpleasant taste by adding flavors and sweeteners. A new approach has been the development of bitter blockers based on the biology of taste.

There are significant age-related differences in how children and adults respond to flavors. Therefore, adult sensory panels may not be able to predict flavors that children prefer and those they will reject. The use of taste sensing analytical devices (electronic tongues) for initial screening of foods and beverages in children is still in its infancy. The advantages of this approach include its speed, relatively low cost, and lack of risk. The use of this technology has so far not been validated in children.

Implications for psychophysical testing as well sensory evaluation methods for children have been published in standard guides and review articles. There are, however, no peer-reviewed research studies that systematically determined the validity of many of these methods among children of varying ages. Cultural groups also differ in their sensitivity and preference for bitter tastes and other flavors. The lack of acceptable and palatable dosage forms is a major reason responsible for the low rates of adherence in children, and has been implicated as the major reason for pediatric hospital readmissions with treatment failures. Adolescents with chronic diseases (e.g., diabetes, asthma, post solid-organ transplantation) have significant and potentially life-threatening lack of adherence.

In addition to drugs administered orally, other routes of administration are being used in children with varying degrees of success. With the advent of the needle-free injections, devices for parenteral drug delivery can now be grouped into invasive and non-invasive categories. Neonates require the use of invasive delivery systems and formulations providing appropriate concentrations and volumes. The use of potentially toxic excipients in these populations remains a serious concern in low birth weight infants. It is anticipated that the increased availability of biotechnology-based drugs will require the development of reliable delivery systems using the subcutaneous route. In addition to topically applied pediatric medicines, transdermal patches and iontophoresis technologies have been used in children with limited success. However, transdermal patches may in the future be used for non- invasive delivery of vaccines.

The recent advances in nanoscience and nanotechnology have resulted in the development of nanoparticle-based diagnostic and therapeutic approaches for the treatment of adult cancers, infections, asthma and other conditions. Nanoparticles-based drug delivery have advantages over conventional formulations including increased solubility of poorly water soluble drugs, sustained release of drugs, delivery of drugs to specific targets tissues, and minimizing toxic effects. There is a need to test new drug delivery systems in pediatrics using nano-particle-facilitated delivery. Targeted therapy using anti-cancer and anti-infective drugs encapsulated in nanoparticles, for example, holds considerable promise to reduce toxicity and improve the efficacy of drugs given to children. The rapid advances in peptide and protein pharmacology have fueled great interest in these types of compounds. Although initial attempts have failed (e.g., insulin delivered by inhalation), novel experimental smart polymer-based drug delivery systems have been developed to deliver drugs at a controlled rate over long periods of time. Smart polymers are macromolecules that display significant physicochemical changes in response to small changes in the environment. Major advantages of smart polymer based systems include delivery for site specific action and decreased total body exposure may have significant pediatric applications in the future In vivo nanodevice-based platform which improved efficacy of treatment combined with diagnostics in one construct (theranostics) is being tested in children with cancer.

The delivery of drugs to the lungs or for systemic delivery using inhalers has been limited by the different physiology of children compared with adults (e.g., airway diameter, short respiratory cycle time, and small tidal volume). There is a need for versatile, efficient devices given the variety of treatment modalities needed and the developmental and behavioral characteristics of young children.

Drug administration by the ocular route remains problematic for the treatment of posterior eye diseases.

Scope

Specific areas of research interest include but are not limited to the following:

- Development of innovative technologies and platforms for oral pediatric formulations for poorly soluble drugs, unpalatable drugs, and for drugs requiring reconstitutable dosage forms, including taste masking and the use of novel excipients;
- Use of a materials science approach to overcome solubility limitations of pediatric drugs, increase bioavailability, decrease excipients' exposure, and provide effective taste masking;
- Development of a strategy for the design of solubility enhancing formulations of highly insoluble pediatrics drugs based on physicochemical and molecular interactions of drug/stabilizer system;
- Development of nanosized formulations to optimize efficacy and minimize toxicity of off patent pediatric drugs of narrow therapeutic index;
- Development of appropriate oral pediatric formulations for drugs included for study in the Best Pharmaceuticals for Children Act (BPCA) [Best Pharmaceuticals for Children Act (BPCA) Priority List of Needs in Pediatric Therapeutics (76FR 18228; http//federalregister.gov/a/2011-7673)];
- Development of neonatal parenteral formulations minimizing the excipients known to be toxic for low birth weight infants;
- Development of novel approaches for oral mucosal, transdermal, nasal, pulmonary and parenteral drug delivery systems and device technologies;
- Development of long acting pediatric formulations by combining APIs and proprietary

nanocarriers;

- Performance of studies of the excipients used in pediatric formulations, assessing interaction of excipients with drugs and with other excipients in different pediatric formulations,;
- Development of biodegradable nanoparticles for targeted antibiotic delivery to the site of localized infections.